



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/039,898	01/03/2002	David Lauffer	VPI/98-19 US	8724

7590

06/16/2003

VERTEX PHARMACEUTICALS INCORPORATED  
130 Waverly Street  
Cambridge, MA 02130-4646

EXAMINER
BALASUBRAMANIAN, VENKATARAMAN

ART UNIT	PAPER NUMBER
----------	--------------

1624

DATE MAILED: 06/16/2003

8

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/039,898

Applicant(s)

LAUFFER ET AL.

Examiner

Venkataraman Balasubramanian

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 8-10 and 13-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 11 and 12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5. 6) ☐ Other:

### **DETAILED ACTION**

Claims 1-20 are pending.

#### ***Election/Restrictions***

Applicant's election of Group II, claims 1-20 in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Election of species is also acknowledged.

However, upon further examining the claims, examiner noted an error in the restriction requirement. Hence, following revised restriction requirement is made:

#### ***Election/Restrictions***

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-7, 11-12, drawn to compound of formula I wherein J and K taken together with the two nitrogens form a five-membered ring, namely hydrogenated imidazole, composition and method of use, classified in class 548, subclass 300.1, class 514, subclass 385.
- II. Claims 1-7, 11-12, drawn to compound of formula I wherein J and K taken together with the two nitrogens form a six-membered ring, namely piperazine, composition and method of use, classified in class 544, subclass 358, class 514, subclass 252.12.
- III. Claims 1-7, 11-12, drawn to compound of formula I wherein J and K taken together with the two nitrogens form a seven-membered ring, namely 1,4-

azepane, composition and method of use, classified in class 540, subclass 575, class 514, subclass 211.01.

- IV. Claims 1-7, 11-12, drawn to compound of formula I wherein J and K taken together with the two nitrogens form a hetero ring not provided for in the above three groups, composition and method of use classified in classes various, subclass various depending upon the choice of suitable JK ring. If this group is elected applicant should elect a specific hetero ring bearing JK and the two nitrogens for examination.
- V. Claims 8-10,13-20 drawn to method of use compound of formula I in combination with various neurotrophic factors classified in classes various, subclass various depending upon the choice of suitable JK ring and the neurotrophic factor. If this group is elected applicant should elect a specific hetero ring bearing JK and the two nitrogens along with a specific neurotrophic agent for examination.

The inventions are distinct, each from the other because of the following reasons:

Invention I, II, III and IV are independent and distinct from each other because they are directed to structurally dissimilar compounds that lack common core namely hydrogenated imidazole versus piperazine versus azepane versus numerous other hetero rings bearing at least nitrogens which are optionally further fused. Consequently, the groups have different classifications and require separate prior art searches. They can be made and used independently. Art, which may render obvious or anticipate one of the groups would not necessarily do the same for the other group as evidenced by the

Art Unit: 1624

several prior art cited in the Information Disclosure Statement. Each can support a patent, as the compounds of each group are capable of being utilized alone not in combination with other members listed in the Markush group.

Invention I-IV and V are independent and distinct from each other because they are directed to combination-subcombination of compound of formula I. There is no required combination. Compound of formula I can be used as is for stimulating neuronal regeneration and the various neurotrophic factors of invention V can be used either independently or in combination with any other active ingredients as evidenced by the claim language and the references cited in the Information Disclosure Statement.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-20 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include

Art Unit: 1624

all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Nandakumar Govindaswamy on 6/3/2003 a provisional election was made with traverse to prosecute the previously elected invention of Group II, claims 1-7, 11-12 along with previously elected species for examination. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-7, 11-12 will be examined to the extent they embrace the elected subject matter. Claims 8-10 and 13-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

***Claim Rejections - 35 USC § 112***

Art Unit: 1624

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 and 11-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim.

1. Recitation of the phrase "derivatives thereof" in claim 1, renders the claim indefinite, as the term "derivative" can be more than what is being positively recited therein. Note the term "derivative" can include any or all organic group and hence the scope of the claim is unclear.
2. The proviso in claim 1 is indefinite as it recites "when J is hydrogen..." . Note J cannot be hydrogen as per the definition on page 30. Hence, It is not clear what this proviso excludes is.
3. Method of use claims 11-12 lack therapeutically effective amount and therefore reads on any or all amount.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Saikawa et al. US 4,379,152.

Saikawa et al teaches several piperazinone compounds used as intermediates for making cephalosprins. See bonding moiety shown in column 1, line 55 and note the definition of various variable groups. See also formula VIII, which corresponds to instant compound when G is absent and D is hydrogen. See Table 1-28 for various piperazinone compounds used as intermediates. Although most of these compounds have chloroformyl group on the nitrogen, as seen in the specification they are made form the corresponding piperazinone compound where the second nitrogen has hydrogen. Hence it is held that in order to make compound shown in these tables Saikawa et al. had inherently made the intermediate, which is claimed in the instant claims. Note In re Petering et al 133 USPQ 275; In re Schaumann, 195 USPQ 5.

Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Silverman et al. US H2007 H.

Silverman et al., teaches several piperazine compounds used as intermediates for making insecticides. See formula shown in column 1, line 20 and note the definition



Art Unit: 1624

of various variable groups. See also formula F in column 4, line 65, which corresponds to instant compound when G is absent and D is hydrogen and formula O in column 6, line 10. See Example 1 on column 6-7 and Table I for various piperazine compounds used as intermediates.

Claims 1 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Hori et al. JP 50 130773, CA 85: 33075, 1976, cited in the Information Disclosure Statement.

See abstract for the compound taught as analgesics.

Claims 1 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Choi et al. J. Med. Chem. 42(18) 3647-3657 cited in the Information Disclosure Statement.

Choi et al. teaches several dopamine transport inhibitors, which includes instant compounds. See examples 24-27.

Claims 1 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Hori et al. JP 50 130773, CA 85: 33075, 1976, cited in the Information Disclosure Statement.

See compounds 4-10, which are useful as anthelmintics.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Chambers et al. WO 97 16446 cited in the Information Disclosure Statement.

Chambers et al., teaches several piperazine compounds used as intermediates for making 5HT<sub>1</sub> receptor activity. See formula XI on page 22 and examples on pages 37-53.

Claims 1, 7, 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Pascal et al. EP 0 289 227 cited in the Information Disclosure Statement.

Pascal et al., teaches several piperazine compounds useful for treating various neurodegenerative diseases. See formula A on page 4 and examples on pages 37-53.

### ***Claim Objections***

Claims 11-12 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot dependent on another multiple dependent claim. Note claim 11 depends any one of claims 1-6 and claim 3 is a multiple dependent claim. See MPEP § 608.01(n).

References cited in the Information Disclosure Statement (paper #5) are made of record.

### **Conclusion**

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (703) 308-4716. The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

*V. Balasubramanian*  
Venkataraman Balasubramanian

6/13/2003